### PATENT COOPERATION TREATY

PCT/IL2008/001492

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### From the INTERNATIONAL BUREAU

## **PCT**

NOTIFICATION CONCERNING
TRANSMITTAL OF COPY OF INTERNATIONAL
PRELIMINARY REPORT ON PATENTABILITY
(CHAPTER I OF THE PATENT COOPERATION
TREATY)

(PCT Rule 44bis.1(c))

| G.E. EHRLICH (1995) LTD. |
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| Date of mailing (day/month/year) 27 May 2010 (27.05.2010) |            |   |   |
|---|------------|---|---|
| Applicant's or agent's file reference 45192               |            |   | IMPORTANT NOTICE  |
| International application No.<br>PCT/IL2008/001492        |            | ate (day/month/year)<br>2008 (13.11.2008) | Priority date (day/month/year)<br>15 November 2007 (15.11.2007) |
| Applicant   | SENG ENTER | PRISES LTD. et al                         |   |

The International Bureau transmits herewith a copy of the international preliminary report on patentability (Chapter I of the Patent Cooperation Treaty)

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Authorized officer

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### PATENT COOPERATION TREATY

## **PCT**

# INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY (Chapter 1 of the Patent Cooperation Treaty)

(PCT Rule 44bis)

| 45192   | FOR FURTHER ACTION   | See item 4 below  |
|---|--|---|
|   | International filing date (day/month/year) 13 November 2008 (13.11.2008) | Priority date (day/month/year)<br>15 November 2007 (15.11.2007) |
| International Patent Classification (8th e<br>See relevant information in Form PC | edition unless older edition indicated)<br>CT/ISA/237                    |   |
| Applicant<br>SENG ENTERPRISES LTD.  |  |   |

| 1.     | This international preliminary report on patentability (Chapter 1) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 bis.1(a).                               |  |   |   |  |
|--------|---|--|---|---|--|
| 2.     | This REPORT consists of a total of 7 sheets, including this cover sheet.  |  |   |   |  |
|        | In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead. |  |   |   |  |
| 3.     | This report contains indications relating to the following items:   |  |   |   |  |
|        | $\boxtimes$   | Box No. I  | Basis of the report   |   |  |
|        |   | Box No. II Priority  |   |   |  |
|        |   | Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability |   |   |  |
|        |   | Box No. IV   | Lack of unity of invention  | 1   |  |
|        | $\boxtimes$   | Box No. V  | Reasoned statement under applicability; citations and             | r Article 35(2) with regard to novelty, inventive step or industrial dexplanations supporting such statement                                |  |
|        | $\boxtimes$   | Box No. VI   | Certain documents cited   |   |  |
|        |   | Box No. VII  | Certain defects in the international application                  |   |  |
|        |   | Box No. VIII   | Certain observations on the international application             |   |  |
| 4.     | The Interr<br>not, excep<br>date (Rule  | t where the applicar   | communicate this report to des<br>it makes an express request und | ignated Offices in accordance with Rules 44bis.3(c) and 93bis.1 but ler Article 23(2), before the expiration of 30 months from the priority |  |
|        |   |  |   |   |  |
|        | <u> </u>  |  |   | Date of issuance of this report<br>18 May 2010 (18.05.2010)   |  |
|        |   | The International Bu   |   | Authorized officer  |  |
|        |   | 34, chemin des C<br>1211 Geneva 20,  |   | Simin Baharlou  |  |
|        | e-mail: pt09.pct@wipo.int   |  |   |   |  |
| rorm l | C1/1B/3/3   | (January 2004)   |   |   |  |

| P   | ATENT COOPE  | RATION TREA  | TY   |
|---|--|--|--|
| From the INTERNATIONAL SEARCHING AUTHO  | RITY   | •  |  |
| To:<br>G.E. EHRICH (1995)LTD.<br>11 MENACHEM BEGIN STREET<br>52521 RAMAT GAN<br>ISRAEL          |  |  | PCT  |
|   |  | WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY |  |
|   |  |  | (PCT Rule 43bis.1)   |
|   | -  | Date of mailing (day/month/year)                         | 13 MAY 2009  |
| Applicant's or agent's file reference   | •  | FOR FURTHER A  |  |
| 45192   | <u> </u>   |  | See paragraph 2 below  |
| International application No.   | International filing date                          |  | Priority date (day/month/year)   |
| PCT/IL 08/01492   | 13 November 2008                                   |  | 15 November 2007 (15.11.2007)  |
| International Patent Classification (IPC) o<br>IPC(8) - C12M 3/00 (2009.01)<br>USPC - 435/305.2 | r both national classifica                         | tion and IPC   | 1  |
| Applicant SENG ENTERPRISES  | LTD.   |  |  |
| This opinion contains indications rela  | sting to the following its                         |  |  |
| Box No. I Basis of the op   |  | nis:   |  |
| Box No. II Priority   |  |  |  |
| 1 =   | tent of opinion with rem                           | ed to novelty inventiv                                   | e step and industrial applicability  |
| Box No. IV Lack of unity o  |  | in to noverty, investiga-                                | c step and industrial applicationty  |
| Box No. V Reasoned states   |  | a)(i) with regard to nov                                 | elty, inventive step or industrial applicability;  |
| Box No. VI Certain docum  |  |  |  |
| Box No. VII Certain defects in the international application                                    |  |  |  |
| Box No. VIII Certain observa  | ations on the internations                         | al application   | ·  |
| 2. FURTHER ACTION   |  |  |  |
| International Preliminary Examining   | Authority ("IPEA") exce<br>id the chosen IPEA has: | ept that this does not ap<br>notified the Internation    | be considered to be a written opinion of the ply where the applicant chooses an Authority all Bureau under Rule 66.1 bis(b) that written |
| If this opinion is, as provided above,  | considered to be a writte                          | n opinion of the IPEA, before the expiration             | the applicant is invited to submit to the IPEA of 3 months from the date of mailing of Form it expires later.                            |
| For further options, see Form PCT/IS  |  |  | •  |
| 3. For further details, see notes to Form   | PCT/ISA/220.                                       |  | -  |
|   | 1  | · · · · · · · · · · · · · · · · · · ·                    |  |
| Name and mailing address of the ISA/US Mail Stop FCT, Attn: ISA/US                              | Date of completion of                              | this opinion   | Authorized officer:  |
| Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450                         | 30 April 2009 (30                                  | .04.2009)  | Lee W. Young   |
| Facsimile No. 571-273-3201 PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774                     |  |  |  |

Form PCT/ISA/237 (cover sheet) (April 2007)

International application No.

PCT/IL 08/01492

| Box | No. I   | Basis of this opinion  |
|-----|---------|--|
| i.  | With r  | egard to the language, this opinion has been established on the basis of: the international application in the language in which it was filed.   |
| :   |         | a translation of the international application into which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b)).   |
| 2.  |         | This opinion has been established taking into account the rectification of an obvious mistake authorized by or notified to this Authority under Rule 91 (Rule 43bis.1(a))  |
| 3.  | establ. | regard to any nucleotide and/or amino acid sequence disclosed in the international application, this opinion has been ished on the basis of:   |
|     | a. tyj  | pe of material   |
|     | _<br>   | a sequence listing   |
|     |         | table(s) related to the sequence listing   |
|     | b. fo   | rmat of material   |
|     | Ξ       | on paper   |
|     |         | in electronic form   |
|     |         |  |
|     | c. tir  | ne of filing/furnishing  |
|     | Ļ       | contained in the international application as filed  |
| Ì   | <br> -  | filed together with the international application in electronic form   |
|     |         | furnished subsequently to this Authority for the purposes of search  |
| 4.  |         | In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished. |
| 5.  | Addit   | ional comments;  |
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International application No.

PCT/IL 08/01492

| Box No. IV Lack of unity of invention  |
|--|
| 1. In response to the invitation (Form PCT/ISA/206) to pay additional fees the applicant has, within the applicable time limit:  |
| paid additional fees   |
| paid additional fees under protest and, where applicable, the protest fee  |
| paid additional fees under protest but the applicable protest fee was not paid   |
| not paid additional fees   |
| 2. This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.  |
| 3. This Authority considers that the requirement of unity of invention in accordance with Rule 13.1, 13.2 and 13.3 is  |
| complied with  |
| not complied with for the following reasons:  This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.  |
| Group I: claims 1-11, 25-36 and 48-51, directed to a holding device for cells comprising an array of spaced picoliter wells, further wherein the holder may be translucent.  Group II: claims 12 and 13, directed to a method of forming a template for a picoliter well array.  Group III: claims 14-24 and 37-47, directed to a method of forming a cell holding device having an array of picoliter wells.  |
| The inventions listed as Groups I - III do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:  |
| The special technical feature of the Group I claims is a holding device for cells comprising an array of spaced plooliter wells. The special technical feature of the Group II claims is a method of forming a template for a picoliter well array. These special technical feature of the Group III claims is a method of forming a cell holding device having an array of picoliter wells.   |
| The only common technical element shared by the above groups is that they are related to an array of wells having picoliter volume. This common technical element does not represent an improvement over the prior art of US 2004/0219074 A1 to Childers et al. (see para [0015], [0028]) Therefore, the inventions of Groups I-III lack unity of invention under PCT Rule 13 because they do not share a same or corresponding special technical feature. |
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| 4. Consequently, this opinion has been established in respect of the following parts of the international application:   |
| ali parts  |
| the parts relating to claims Nos. 1-11, 25-36 and 48-51  |

International application No.

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| Box No. V   | Reasoned statement un<br>citations and explanation  | der Rule 43 <i>b</i><br>ons supportin  | is.1(a)(i) with regard to novelty, inventive step or industrial applicang such statement   | ıbility;     |
|---|---|--|--|--------------|
| 1. Statemen   | ıt  |  |  |              |
| Novel   | lty (N)   | Claims<br>Claims   | 1-6, 11, 34-36<br>7-10, 25-33, 48-51   | YES<br>NO    |
| laven   | tive step (IS)  | Claims<br>Claims   | NONE<br>1-11, 25-36, 48-51   | YES<br>NO    |
| Indus   | trial applicability (IA)  | Claims<br>Claims   | 1-11, 25-36, 48-51<br>NONE   | YES<br>NO    |
| As to claim 7, 8 (para [0142]; Fig (a) a pico liter w (b) a non-cell ho                         | enn discloses a holding de<br>g 31):<br>rell array region including a<br>olding region (para [0068];<br>n fluid can be one or both a                                | vice (para [00<br>plurality of pic<br>Fig. 6 part 64)  | ng anticipated by US 2005/0277125 A1 to Benn, et al. (hereinafter *Ben<br>076]-[0077]) for studying cells (para [0113]) comprising at least two defin<br>co liter wells (para [0280]; Fig 6); and<br>) in fluid communication (para [0159]; Fig 31) with seld pico liter well reg<br>noved from said non cell holding region without disturbing cells in said pi   | ed regions   |
| As to claim 8, 8<br>[0159], disclosir   | enn further discloses at lea<br>ng a blind hole; Fig 31, parl   | ist one fluid pi<br>98) between  | ermeable (para [0099], [0110], disclosing porous reaction surfaces) barr<br>said regions (Fig 31, part 98).  | ier (para    |
| As to claim 9, 8  | enn further discloses wher  | e the non-cell   | holding array has an embossed design (para (0170]).  |              |
| _   |   |  | er well array is embossed (para [0170]).   |              |
| Claims 25-33 au<br>"Deutsch").  | nd 48-51 lạck novelty unde  | r PCT Article  | 33(2) as being anticipated by WO 2005/007796 A2 to Deutsch, et al. (he   | ereinafter   |
| essentially of ware the cavity has plastics, or rubb — wherein the — wherein the — the substrat | ater (pg 49, in 3-19, disclos<br>aving a substrate (pg 11, ir<br>er),<br>substrate includes a surfa<br>surface includes a multipli<br>te is substantialiv transluce | sciosing picow<br>sing 99% waten<br>25-31) and a<br>ce for receiving<br>city of pico lite<br>of (eq. 17, lo.1) | generally inert wall (pg 10, in 18-26, disclosing a wall made of ceramic, ing the medium (pg 12, in 1-15), and proved in the state of t | consisting   |
| As to claim 26,   |   | vhere the med  | dium comprises water (ng 49 in 3-19 disclosing 99% water ash disco   | nd wherein   |
| As to claim 27,   | Deutsch further discloses v   | vhere the sub:   | strate is moldable (pg 33, ln 16-20, disclosing a device made through m  | iolding).    |
|   |   |  | strate is inert (pg 45, in 4-14).  | ŭ,           |
| As to claim 29, is disposed beto  | Deutsch further discloses veen the carrier plate and  | vhere the hold<br>the substrate (  | ding device is a carrier plate (pg 6, tn 24 to pg 7, ln 3) and wherein a first (pg 43, ln 5-11; Fig 15A-15C).  | t adhesive   |
| As to claim 30,<br>Fig 14A-14C).  | Deutsch further discloses a   | second adhe  | esive disposed between the generally inert wall and the substrate (pg 42   | ?, In 20-28; |
| As to claim 31, curable (pg 42,   | Deutsch further discloses v<br>In 20-28, disclosing light-ca  | vhere at least<br>Irable adhesiv   | one of the substrate, the first adhesive and the second adhesive are UV ve 3051).  | √-light      |
| As to claim 32, curable adhesiv   | Deutsch further discloses v<br>e 3051, an acrylic adhesiv   | where the first<br>e).   | adhesive and the second adhesive are acrylic (pg 42, in 20-28, disclosi  | ing light-   |
| ******  | ***********See Suppleme   | ntal Sheet to o  | continue************************************   |              |

International application No.

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### Supplemental Box

In case the space in any of the preceding boxes is not sufficient. Continuation of: BOX V(2):

As to claim 33, Deutsch further discloses a light source transmitting the UV-light through a bottom surface of the at least one cavity (pg 42, In 20-28; Fig 14B).

As to claim 48, Deutsch discloses a holding device (pg 6, in 27-28, disclosing a holder) for studying cells (pg 1, in 4-5) comprising:

- a layer (pg 12, in 1-15) of substantially transparent substrate material (pg 17, in 19-26);
  having a multiplicity of pico liter wells (pg 12, in 1-15; Fig 10A-10C);
  having a refractive index of 1.33 (pg 12, in 10-15); and,
  a wall structure attached to the substrate (Fig 15A-15C).

As to claim 49, Deutsch further discloses where the substrate is UV-light curable (pg 13, in 8-20; pg 39, in 12-18).

As to claim 50, Deutsch further discloses a first adhesive disposed between the wall structure and the substrate (pg 43, in 5-11; Fig 15A-15C).

As to claim 51, Deutsch further discloses

- a substantially transparent carrier plate (pg 6, in 23-27; pg 17, in 19-26; Fig 13-16);
- having a plurality of cavities (pg 50, In 14-19, disclosing picowalls) surrounded by walls formed in a first surface of the carrier plate (Fig 13-16),
- wherein the layer of substantially transparent substrate material is disposed on the carrier plate (pg 6, in 23-27; pg 17, in 19-26; Fig 13-16).

Claims 1-6 and 11 lack an inventive step under PCT Article 33(3) as being obvious over Benn in view of US 2005/0026299 A1 to Bhattacharjee, et al. (hereinafter "Bhattacharjee").

As to claim 1, Benn discloses a holding device (para [0076]-[0077]) for studying cells (para [0113]) comprising a spaced apart (para [0279]) pico liter wells (para [0280]). Bonn does not specifically disclose a pturality of arrays. Bhattacharjee discloses a holding device for studying cells (Abstract; para [0066]) comprising a plurality of arrays (para [0007]; Fig 4, 5, 11B). It would have been obvious to a skilled artisan to combine the Benn and Bhattacharjee disclosures by using a plurality of the arrays taught by Benn on a holder. A skilled artisan would have been motivated to combine the references by the Bhattacharjee disclosure, suggesting such a configuration will provide benefits in fluid handling (para [0008]).

As to claim 2, Benn further discloses where the pico liter well arrays comprise embossed regions (para [0170]).

As to claim 3, Benn further discloses ploo liter well arrays (para [0280]). Bhattacharjee further discloses at least one barrier (para [0049], disclosing scores; Fig 11B) between two arrays (Fig 11B).

As to claim 4, Benn further discloses where the arrays are arranged in a two dimensional repeating pattern (para [0295]; Fig 19).

As to claim 5, Bhattacharjee further discloses where the arrays include at least two different well array designs (para [0011]; Fig 1, 2).

As to claim 6, Benn further discloses where the device includes at least one non-well embossed region (para [0158], disclosing a transfer plate) fluidically connected to at least one of said arrays (para [0159]).

As to claim 11, Benn further discloses pico liter well arrays (para [0280]). Benn does not specifically disclose a plurality of well array regions. Bhattacharjee discloses a holding device for studying cells (Abstract; para [0066]) comprising a plurality of well array regions (para [0007]; Fig 4, 5, 118). It would have been obvious to a skilled artisan to combine the Benn and Bhattacharjee disclosures by using a plurality of the array regions taught by Benn on a holder. A skilled artisan would have been motivated to combine the references by the Bhattacharjee disclosure, suggesting such a configuration will provide benefits in fluid handling (para [0008]).

Claims 34 and 35 lack an inventive step under PCT Article 33(3) as being obvious over Deutsch in view of US 4,684,538 A (Klemarczyk).

As to claim 34, Deutsch does not specifically disclose where the substrate is exposed to UV-light under vacuum pressure. Klemarczyk discloses an adhesive that is attached to a substrate (col 1, in 50-62), where the adhesive is cured by exposing it to the UV-light (col 13, in 62 to col 14, in 4) under vacuum pressure (col 14, in 7-25). It would have been obvious to a skilled artisan to combine the Deutsch and Klemarczyk disclosure by curing the adhesive taught by Deutsch under UV light and vacuum pressure. A skilled artisan would have been molivated to combine the references by the Deutsch disclosure, suggesting the use of a light-curable adhesive (pg 42, In 20-28).

As to claim 35, neither Deutsch nor Kiemarczyk specifically discloses where the vacuum pressure is in the range of 0.3-0.5 mmHg. However, such a range would have been obvious to a skilled artisan practicing the Deutsch and Klemarczyk disclosures through normal experimentation. A skilled artisan would have been motivated to use such a range in order to cure certain adhesives with different properties than those disclosed by Klemarczyk,

| See the following Supplemental Sheet to continue************************************ | ****** | ***** | ****** |
|--|--------|-------|--------|
|  |        |       |        |

International application No. PCT/IL 08/01492

| Supplemental Box   |  |  |
|--|--|--|
| In case the space in any of the preceding boxes is not sufficient.  Continuation of: BOX V(2) and the preceding Supplemental Sheet:  |  |  |
| Claim 36 lacks an Inventive step under PCT Article 33(3) as being obvious over Deutsch in view of US 3,558,387 A to Bassemir, et at (hereinafter "Bassemir").  |  |  |
| As to claim 36, Deutsch does not specifically disclose where the substrate is exposed to the UV-light under inert gas. Bassemir discloses a curing adhesive (col 4, In 58-69) where an adhesive is exposed to the UV-light (col 2, In 52-58) under inert gas (col 3, In 65-68). It would have been obvious to a skilled artisan to combine the Deutsch and Bassemir disclosures by using method disclosed by Bassemir with the light-curing adhesive taught by Deutsch. A skilled artisan would have been motivated to use such a method by the Bassemir disclosure, suggesting that curing the adhesive in an inert atmosphere reduces curing time (col 4, in 32-34). |  |  |
| Claims 1-11, 25-36, and 48-51 have industrial applicability as defined by PCT Article 33(4) because the subject matter can be made or used in industry.  |  |  |
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